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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,210	02/24/2004	Robert M. Strom	62424A	1668

109 7590 10/20/2004

THE DOW CHEMICAL COMPANY
INTELLECTUAL PROPERTY SECTION
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EXAMINER	
MAYER, SUZANNE MARIE	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/785,210	STROM ET AL.	
	Examiner	Art Unit	
	Suzanne M. Mayer, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5-24-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-22 are pending in this application and thus have been examined and considered in this Office action.

Priority

2. The claim for priority of US application number 10/373,306 is acknowledged. However, an application in which the benefits of an earlier application are desired must contain a specific reference to the prior application in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. Appropriate correction is required.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on May 24, 2004 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner. See attached PTOL-1449.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not include the notary's signature, or the notary's signature is in the wrong place.

It does not include the notary's seal and venue.

Specification

5. The disclosure is objected to because of the following informalities. Paragraphs 10 and 28 disclose a sequence for D2A21 and D4E1, however, it is not disclosed in the sequence listing with and appropriate sequence identifier (e.g. SEQ ID No:).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear in claims 1, 10, 15, and 20 what the antimicrobial peptide activity of IC50 of $\leq$125 μg/mL is intended to act upon. A specific

organism for which the IC50 refers is necessary. It has no meaning without a specific target, and conditions. Claims 2-22 are included in this rejection because they do not remedy the rejection of claim 1.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-15 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims read on an enormous variation and number of peptides made up of repeating identical units consisting of 2, 3, or 4 hydrophobic or cationic amino acids which may or may not possess any antimicrobial activity whatsoever and a process of manufacturing these peptides. Thus, the claims read on almost an infinite number of peptide possibilities. The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to all of the possible peptides with repeating identical monomeric units of 2,3, or 4 amino acids comprised of any

combination of hydrophobic and cationic residues and a method of how to produce these peptides.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case, the claims read on an enormous number of possible peptides that may or may not possess any antimicrobial activity whatsoever. In determining if the peptides have any antimicrobial activity, it would be necessary for a skilled artisan to either synthetically or recombinantly produce the peptides according to the claimed invention which is represented by identical repeating monomers that consist of 2, 3 or 4

amino acid comprised of %25-75 cationic residues with the rest being hydrophobic residues and which ideally posses from 14-80 residues. However, the specification while maintaining that the invention comprises a novel process for producing periodic peptides (see p. 1, paragraph 3) does not provide *any* guidance whatsoever in how to prepare these peptides according to the invention and does not provide *any* working examples of this process. Furthermore, applicants in their quest to test the activities of the antimicrobial peptides according to their own invention, which are represented by SEQ ID Nos: 1-56, ordered their periodic antimicrobial peptides from 'a known manufacturer' (see p. 6, paragraph 25). Furthermore, it is unclear whether any cationic residue or any hydrophobic residue which is manufactured or created according to the present invention will possess antimicrobial activity. It would therefore, require a skilled artisan to further perform additional experiments in order to ascertain whether all of the different conceivable different peptides functioned as antimicrobial peptides. For example, if a repeating monomeric subunit of HGGH were used, would this peptide possess antimicrobial activity? The state of the prior art suggests that it would not. Chen et al. teach that, at least for antibacterial cationic peptides, that the inclusion of arginine lysine, tryptophan or isoleucine residues enhances the effectiveness against certain bacteria. Furthermore, the predictability whether any or all of the peptides made according to the claimed invention possessed antimicrobial activity would is non-existent. There is no way for one to predict the effectiveness without further experimentation when the claims are interpreted in their broadest sense which makes the instant claims an invitation for undue and unnecessary experimentation.

10. Claims 1-15 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to antimicrobial peptides which consist of identical repeating monomeric units comprised of various combinations of 2, 3 or 4 cationic or hydrophobic amino acids in a peptide that is 14-80 amino acids long and having at least an IC50 of $\leq$ 125 μg/mL. However, the huge amount of possibilities and combinations of peptides which this generic formula encompasses makes it clear that Applicant could not have had in their possession at the time of filing every single possible combination or peptides which fit this general formula. Furthermore it is unclear whether or not each and every peptide, which follows this formula would actually possess antimicrobial activity. For example, would a peptide with a monomeric unit of (His-Pro-Pro-His) possess antimicrobial activity? The state of the prior art suggests it may not. Chen et al. teach that when constructing effective antibacterial peptides that the inclusion of the cationic residues of arginine and lysine as well as the hydrophobic residues of tryptophan or isoleucine enhances the effectiveness of the peptides against various bacteria. The specification does not describe the combinations of all of the possible cationic residues in combination with all of the hydrophobic residues. Rather, what is clearly described is the following: the cationic residues of arginine and lysine, in combination with the hydrophobic residues of phenylalanine, alanine, leucine, glycine

and threonine and the effectiveness of these peptides which are represented by SEQ ID Nos: 1-56.

Vas-Cath Inc. V. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As discussed above, the skilled artisan cannot envision the detailed structure of the encompassed genus of polypeptides, and therefor conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bazile et al.

Bazile et al. disclose in column 2, lines 33-36, SEQ ID Nos: 3 and 4, where the general formula is identified as (LKKL)n and (LKLK)n, respectively, and where n is defined as being an integer equal to or greater than four. Therefore two these general formulae anticipate SEQ ID Nos: 15-18 of the instant application, which corresponds to the Bazile et al. general formula of SEQ ID No: 3, when n is equal to 5-8, respectively; and SEQ ID Nos: 44, 46 and 48-50 of the instant application, which correspond to SEQ ID No: 4 of Bazile et al., when n is equal to 4-6, 9 and 12, respectively, and the broad generic formulas disclosed in claims 1-15.

13. Claims 1-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Seipke et al. Seipke et al. discloses oligopeptides of the following formula (Lys-Phe-Lys)n where n is equal to 3-9 (see p. 268, 2nd column, 1st paragraph and Table 1 on p. 270). Therefore, this formula anticipates SEQ ID No: ID Nos: 24-29 and the broad generic formulas disclosed in claims 1-15.

Conclusion

14. No claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Mayer, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached Monday to Friday from 8.30am to 5.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMM
15 October, 2004

JON WEBER
SUPERVISORY PATENT EXAMINER